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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/169,048	10/08/98	HUSE W	P-IX-3280

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EXAMINER	
GARCIA,M	
ART UNIT	**PAPER NUMBER**
1627	16

DATE MAILED: 11/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File copy

Office Action Summary

Application No.	Applicant(s)
09/169,048	Huse et al
Examiner	**Group Art Unit**
Maurie E. Garcia, Ph. D.	1627

☒ Responsive to communication(s) filed on *Sep 5, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *THREE* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-38* is/are pending in the applicat

Of the above, claim(s) *1-9 and 19-38* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *10-18* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5 & 7*

☒ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's Response filed September 5, 2000 (Paper No. 14) is acknowledged. No claims were cancelled, added or amended and therefore claims 1-38 are pending.

Restriction/Election

2. Applicant's election with traverse of Group II (Claims 10-18) is acknowledged. The traversal is addressed below. Also, as requested, the examiner called applicant to discuss the traversal. An Interview Summary form detailing this discussion is attached to this action.

3. Applicants traverse the Restriction Requirement with respect to the separation of the claims of Group I from Group II and state that combined search and examination would not create an undue burden. However, the examiner maintains that the inventions are distinct since they are different methods. As stated in the restriction requirement, the methods are different because they use different steps, require different reagents and will produce different products and/or results. Group I involves the use of a collective receptor variant population and Group II involves the use of a collective ligand variant population, which represent different starting materials. Also, Group II is drawn to determining binding to one or more receptors and Group I is drawn to determining binding to one or more ligands. Again, there is no expectation that the searches of these two groups would be coextensive. Therefore, this does create an undue search burden. The requirement is still deemed proper and is therefore made FINAL.

4. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement between Groups III-V, the election has been treated as an election without traverse (MPEP § 818.03(a)) with respect to these groups.

5. Claims 1-9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 14 (for Group I, claims 1-9).

6. Claims 19-38 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions. Election was made **without** traverse in Paper No. 14 (for Groups III-V, claims 19-38).

7. Therefore, claims 10-18 are examined on the merits.

Sequence Compliance

8. The examiner thanks applicant for the submission of a corrected Sequence Listing on March 28, 2000. This has been verified as error-free and has been entered into the instant case.

Specification

9. The disclosure is objected to because of the following informalities:

On page 54, line 18 of the specification, a "Figure 6" is referred to; however, there are only four figures in the instant application. Appropriate correction is requested.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 10-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a method of determining binding of a "ligand" to one or more "receptors". The claims use generic terminology such as "collective ligand variant population", "binding activity" and "optimal binding affinity". These terms are defined in the instant disclosure but the definitions are very broad.

The specification discloses **no** examples of carrying out such a method (the only example given appears to be for the opposite case scenario). These ligands and receptors could encompass very different moieties such as peptides, oligonucleotides or other organic molecules. Also, claims 15 and 16 require specific techniques of

producing the ligands (recombinant expression in melanophore cells) and claim 17 requires tagging with an "identifiable tag". None of these techniques are adequately described in the instant disclosure. There are **no** examples of producing ligands by recombinant expression in melanophore cells and **no** examples of tagging such ligands whatsoever.

Thus, the disclosure simply does not provide adequate support to show possession of the claimed invention. The disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned. This further evidences that instant disclosure does not constitute support for the claimed genus or a substantial portion thereof.

12. Claims 10-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;

(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims and the nature of the invention: The claims are drawn to a method of determining binding of a "ligand" to one or more "receptors". No limitations on the specific structure of the ligand or receptor are given and, as such, this could read on a wide variety of structures. The invention is such that each of the components must be present in operable form for successful practice of the invention. For example, the ligand must bind the receptor and the binding must be able to be detected. The state of the prior art and the level of predictability in the art: Ligand/receptor binding pairs were well-known in the art at the time of the invention (see art rejections below); however, only limited numbers of such pairs were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of *any* such pair of molecules. The structures of possible variants are sufficiently diverse that one of ordinary skill would not be able to predict their structures. Also, claims 15 and 16 require specific techniques of producing the ligands (recombinant expression in melanophore cells) and claim 17 requires tagging. All of these techniques are unpredictable in the art. One of ordinary skill would not know, a priori, how to make such a ligand by the claimed method and also how to tag such a ligand with an "identifiable tag". Specifically, in regard to claims 15 and 16, it was known in the art at the time of filing how to make *receptors* using melanophore

cells (see US 5,462,856, on PTO-1449, Examples 1-6 and claims), but not how to make *ligands* in such a manner. With regard to claim 17, adding tags to the ligands adds to the unpredictability of the claimed method since this type of synthesis requires high efficiency and is further complicated by carryover, cross-reactions, etc., all of which are acknowledged issues in the art. Each must be dealt with in the optimization of a synthesis scheme. A review article published by Janda discusses these issues (see Proc. Natl. Acad. Sci. Vol. 91 pp. 10779-10785, November 1994. See especially page 10782-10785). The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. The existence of working examples and the quantity of experimentation needed to make or use the invention based on the content of the disclosure: Applicants have provided **no** working examples of the claimed method, for both the generic embodiments (claims 10-14 and 18) or the specific embodiments (claims 15-17). The state of the prior art is such that one of ordinary skill could not predict how to produce the required ligands and receptors and practice the claimed method of determining binding as required by the instant claims. Therefore further research would be necessary to make or use the invention and it would require undue experimentation to carry out the invention as claimed.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "identifiable" in claim 14 is a relative term which renders the claim indefinite. The term "identifiable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. That is, what constitutes "identifiable" in the context of the claimed tag?

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

16. Claims 10-14, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Combs et al (JACS, January 1996, Vol. 118, No. 1, pp. 287-288).

Combs et al disclose a method for using a "a library of ligands that direct non-peptide binding elements into the specificity pocket of SH3 proteins" (see Figure 1). These ligands comprise two binding sites; "a common low affinity biasing sequence PLPPLP" and 32 "capping reagents" that have the potential to bind in the specificity

pocket (see page 287). The SH3 domain from the protein kinase Src is the receptor. The compounds were assayed against this receptor and at least 7 ligands were identified that bind (see Figure 3 and Table 1). Ligand 1A was also measured against the SH3 domain in the p85 component of PI3K and did show binding for this domain (a second receptor), although it showed selectivity for Src SH3 (see page 288, 2nd column).

The reference discloses that the compounds of the library were tagged and then decoded to find an optimal binding ligand (Figure 3 and Table 1) and the binding of the library compounds (ligands) to the receptor was performed in three stages (see page 287, 2nd column, bottom and Supplemental pages 1-3). This reads directly on the limitations of the instant claims 11-14, 17 and 18.

17. Claims 10-14 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilson-Lingardo et al (On PTO-1449; J. Med. Chem. July 1996, Vol. 39, pp. 2720-2726).

Wilson-Lingardo et al disclose pooling strategies for combinatorial libraries. The reference specifically discloses a method for screening a library of 810 compounds (ligands) for activity towards phopholipase A2 (receptor); see Abstract. An iterative deconvolution method is described in which the library is broken down into smaller and smaller subsets, until a "unique molecule is identified" (reading on the optimal binding ligand of claim 14). This process is described on pages 2721-2722 and in Figure 2, for example. The reference discloses various pooling strategies all of which involve many subsets being made, tested, divided, re-tested and so on

(see, for example Figures 2 and 3 of the reference) reading on the "two or more subpopulations" of claims 11 and 18 and the "dividing, contacting and detecting" of claim 12.

Status of Claims/ Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie E. Garcia, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

20. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DR. JYOTHSNA VENKAT PH.D
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Maurie E. Garcia, Ph.D.
November 17, 2000